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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/303,232	04/30/99	ADAMCZEWSKI M	MO-5176/LEA3

HM12/0203

BAYER CORPORATION
PATENT DEPARTMENT
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EXAMINER	
MAYO,K	
ART UNIT	**PAPER NUMBER**
1633	8

DATE MAILED: 02/03/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/303,232	ADAMCZEWSKI et al.
Examiner	**Group Art Unit**
Kris Pelham Mayo	1633

☒ Responsive to communication(s) filed on *Nov 19, 1999*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-20 and 22-33* is/are pending in the application.

Of the above, claim(s) *8, 9, 11-16, 18-20, 32, and 33* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7, 10, 17, and 22-31* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *7*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Acknowledgment is made of the Preliminary Amendment filed on 04/30/1999, as Paper Number 5, canceling claim 21, and amending claims 1-20.

Claims 1-20, and 22-33 are pending in the instant application.

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-7, 10, 17, and 22-31, drawn to polynucleotides, vectors, host cells, and method of using host cell to make a polypeptide, classified in class 536, subclass 23.2, class 536, subclass 23.5, class 435, subclass 320.1, and class 435, subclass 252.3, for example.

II. Claims 8 and 9, drawn to a polypeptide, classified in class 530, subclass 350, for example.

III. Claims 11 and 32, drawn to an antibody, classified in class 530, subclass 386, for example.

IV. Claims 12-15 and 33, drawn to a transgenic invertebrate, its progeny, and a method of making a transgenic invertebrate, classified in class 800, subclass 13, and class 800, subclass 21, for example.

V. Claim 16, drawn to a method of making a polynucleotide by chemical synthesis, classified in class 536, subclass 25.3, for example.

VI. Claims 18-20, drawn to methods of in vitro assay for compounds that modulate acetylcholine receptor activity, for compounds that bind to acetylcholine receptors, and for compounds that influence expression of acetylcholine receptors, classified in class 435, subclass 4, for example.

Inventions I-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case inventions I-IV are drawn to patentably distinct compositions. The inventions are different because a polynucleotide, vector and host cell, a protein, an antibody, and a transgenic non-human animal all possess materially different physical and chemical properties, structures, and utilities. For instance, a nucleic acid can be used for detecting the presence of mRNA or DNA in a sample, whereas an antibody can be used for detection of a protein. Furthermore, there is nothing on record to indicate that these compositions are obvious variants. As such, the inventions are patentably distinct, and would encompass different search strategies and different considerations. The differences are further underscored by their divergent classification. Inventions V and VI are unrelated to each other and from inventions I-IV because the assay methods and method of making a polynucleotide by chemical synthesis are materially different and plurally independent of the compositions. Furthermore, the assay methods and the method of making the polynucleotide

by chemical synthesis would require different process steps, reagents, and technical considerations. The search for any of the compositions would not be expected to reveal all the references relevant to the methods, and the search for the assay methods would not be expected to reveal all the references relevant to the method of nucleotide synthesis. The search and examination, therefore, would be unduly burdensome.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

A provisional telephonic election was made with traverse, by Mr. Joe Gil on 01/05/2000, to prosecute the invention of group I, claims 1-7, 10, 17, and 22-31. Affirmation of this election must be made by Applicant in responding to this Office Action. Claims 8, 9, 11-16, 18-20, and 32 and 33 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Priority

Acknowledgment is made of Applicant's claim for priority to German Application 19819829.9, filed on 05/04/1998. However, Applicant cannot rely upon the foreign priority papers to overcome the following rejections because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

It is recommended that reference to Applicant's claim for priority be made in the first line of the specification for the sake of clarity.

Information Disclosure Statement

The information disclosure statement filed on 11/19/1999 as Paper Number 7 fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information submitted for consideration by the Office. A copy of the following reference was included, but not listed on the information disclosure statement: Eastham, H.M. et al. "Characterization of a Nicotinic Acetylcholine Receptor from the Insect Manduca Sexta", European Journal of Neuroscience 10:879-889, 1998. The copy of the reference has been placed in the application file, but the information referred to therein has not been considered.

Drawings

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Note the enclosed PTO Form 948 Notice of Draftsperson's Patent Drawing Review outlining the objections to the drawings in the instant application.

Specification

The specification is objected to because it does not conform to the preferred layout and content for patent applications. Applicant is advised on how to arrange the content of the specification. Except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should appear in upper case, without underlining or bold type, as section headings.

Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a). The title of the invention should be placed at the top of the first page of the specification. It should be brief but technically accurate and descriptive, preferably from two to seven words.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) Reference to a "Microfiche Appendix": See 37CFR 1.96(c) and MPEP § 608.05. The total number of microfiche and the total number frames should be specified.

(e) Background of the Invention: The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(f) Brief Summary of the Invention: A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(g) Brief Description of the Several Views of the Drawing(s): A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(h) Detailed Description of the Invention: A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. This item may also be titled "Best Mode for Carrying Out the Invention." Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(i) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet. (37 CFR 1.52(b)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps.

(j) Abstract of the Disclosure: A brief narrative of the disclosure as a whole in a single paragraph of 250 words or less on a separate sheet following the claims.

(k) Drawings: See 37 CFR 1.81, 1.83-1.85, and MPEP § 608.02.

(l) Sequence Listing: See 37 CFR 1.821-1.825.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows: DROP

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7, 10, 17, and 22-31 are rejected under 35 U.S.C. 101 as unpatentable because the claimed invention is directed to non-statutory subject matter. The claims are anticipated by a naturally occurring article which has been deemed as non-statutory, non-patentable subject matter (MPEP 706.03 (a) and 2105). While the Patent and Trademark Office does consider nonnaturally occurring, nonhuman multicellular living organisms, including animals, to be patentable subject matter, it has to be made within the scope of 35 U.S.C. 101. A thing occurring in nature, which is substantially unaltered, is not a "manufacture". See MPEP 706.03(a). In the instant application, the nucleic acid sequences of claim 1 have not been altered by the hand of man in any way, and are a naturally occurring article. Therefore, the nucleic acids of the claims are considered to be directed to non-statutory subject matter. Incorporation of "an isolated nucleic acid" would obviate this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

maintain

Claims 1-7, 10, 17, and 22-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid which comprises a sequence selected from the sequences according to SEQUENCE ID NO: 1, SEQUENCE ID NO: 3, or SEQUENCE ID NO: 5, and partial sequences which are at least 14 base pairs in length of the sequences according to SEQUENCE ID NO: 1, SEQUENCE ID NO: 3, or SEQUENCE ID NO: 5, as are known in the art (Celniker et al./1998, Liao et al./1998, Vogel et al./1998, and Schulte et al./1999), and sequences which exhibit at least 70% identity between position 1295 and position 2195 from SEQUENCE ID NO: 1, or between position 432 and position 1318 from SEQUENCE ID NO: 3, or between position 154 and position 1123 from SEQUENCE ID NO: 5, as are known in the art (Schulte et al./1999), does not reasonably provide enablement for any and all partial sequences which are at least 14 base pairs in length of SEQUENCE ID NO: 1, SEQUENCE ID NO: 3, or SEQUENCE ID NO: 5, or any and all sequences which exhibit at least 70% identity between position 1295 and position 2195 from SEQUENCE ID NO: 1, or between position 432 and position 1318 from SEQUENCE ID NO: 3, or between position 154 and position 1123 from SEQUENCE ID NO: 5. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims, as written, encompass any and all partial sequences which are at least 14 base pairs in length of SEQUENCE ID NO: 1, SEQUENCE ID NO: 3, or SEQUENCE ID NO: 5, and any and all sequences which exhibit at least 70% identity between position 1295 and position 2195 from SEQUENCE ID NO: 1, or between position 432 and position 1318 from SEQUENCE ID NO: 3, or between position 154 and position 1123 from SEQUENCE ID NO: 5.

It would appear that only limited teachings regarding the polynucleotide variability of the claimed invention are found in the specification on page 3, lines 20-30, and page 4, lines 6-8. No references, procedures, or working examples are provided that would enable all these various polynucleotide forms. The claimed variations would drastically alter the polynucleotide, such that the alteration may not result in a functional polypeptide. Even if a functional, biologically active polypeptide results, if it is not functionally equivalent to the insect acetylcholine receptor subunits, then no use is taught for it in the instant application. 70% identity is a low percentage, absent more specific examples, results, evidence or guidance, to ensure that the claimed DNA sequences will encode the desired protein - namely to encode a biologically active insect acetylcholine receptor subunit. Vast numbers of possible sequences are encompassed and there is insufficient enablement or guidance provided in the specification as to what nucleotide insertions, deletions or substitutions could be made to give a partial sequence which is at least 14 base pairs in length, or a sequence which exhibits 70% identity between position 1295 and position 2195 from

SEQUENCE ID NO: 1, or between position 432 and position 1318 from SEQUENCE ID NO: 3, or between position 154 and position 1123 from SEQUENCE ID NO: 5 and still produce a functional insect acetylcholine receptor subunit. The variations could create nonsense, missense or frameshift mutations in the coding sequence that alter the polypeptide encoded by the polynucleotide to the point that it is non-functional. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, such as various sites or regions where the biological activity residues or regions directly involved in binding, stability or catalysis; and in providing the correct three-dimensional spatial orientation for biologically active binding sites, or for sites which represent other characteristics or properties of the protein. These, or other regions, may also be critical determinants of activity. These regions can tolerate only relatively conservative substitutions, or no substitutions. See Bowie et al., 1990. Science, Vol.247, pages 1306-1310, especially page 1306, column 2, paragraph 2; and see Ngo et al., The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz (ed.), pages 433 and 492-495; and Frommel et al/1985). However, Applicant has provided little or no guidance to enable one of skill in the art to determine, without undue experimentation, the positions in the nucleotide and protein which are tolerant to change (ie. such as by amino acid substitutions, insertions or deletions), and the nature and extent of changes that can be made in these positions in order to obtain functional

polypeptides. Such a definition might also read on previously characterized polynucleotides and proteins, or alternatively, might include proteins with additional functions or activities neither envisioned nor enabled by Applicant in the current invention. See Ex parte Forman, 230 U.S.P.Q. 546 (BPAI 1986) with regard to the issue raised above, and In re Fisher, 166 U.S.P.Q. 18. The scope of Applicant's claims encompass modifications on the polynucleotide and protein that would be both critical and non-critical for the biological activity of the polynucleotide and the protein. Thus, even if critical residues in the protein were identified, which in this case they are not, the mere identification of these critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the modified site must assume the proper three-dimensional configuration to be active; that conformation is dependent upon surrounding residues. The substitution/insertion/deletion of non-essential residues can often destroy activity; therefore, it is deemed that to make each of the possible nucleic acid modifications, and resulting amino acid modifications for each of the non-essential residues, even if only conservative replacements were made, would constitute undue experimentation. The introduction of non-conservative substitutions, non-naturally occurring amino acids, deletions, or insertions further raises the possible number or species. Furthermore, it is not clear if the resulting polynucleotide and protein would be the result of one or more of the above modifications; nor is it taught how to go about selecting and choosing which single or multiple combination would produce an encoded functional insect acetylcholine receptor subunit.

Without guidance from the specification as to exactly what variances could occur in the nucleotide sequence, it would necessitate undue experimentation on the part of the skilled artisan to screen all possible variants to determine which have insect acetylcholine receptor subunit functionality. Therefore, all possible variants of the nucleotide sequence that encode a polypeptide, are neither described nor enabled, since the critical sequences that confer functionality to the insect acetylcholine receptor subunits are unknown at this time. Therefore, Applicant has not presented enablement commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 10, 17, and 22-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7, 10, 17, and 22-31 are indefinite in their recitation of "encode the same amino acid sequences as the sequences defined under (a), (b), (c) and (d)" in claim 1(f). The sequences of (a), (b), (c), and (d) are nucleotide sequences, and not amino acid sequences. Therefore, it is not clear what amino acid sequences are being reference in claim 1(f). In the absence of clarity, the metes and bounds of the claimed invention cannot be determined.

Drop

Claim 17 is further indefinite in its recitation of "ensures specific expression". It is not clear what is meant by this term, for example, does it refer to species specific expression, tissue specific expression, or otherwise. In the absence of guidance in the specification, the metes and bounds of the claimed invention cannot be determined.

make new 102/103

Claim 17 is further indefinite in its recitation of the limitation "The regulatory region". There is insufficient antecedent basis for this limitation in the claim. No prior reference is made to a regulatory region in claim 17, or in the independent claim 1, therefore it is not clear what regulatory region is being referenced. In the absence of clarity, the metes and bounds of the claimed invention cannot be determined.

Claim 22 is further indefinite in its recitation of "The nucleic acid of Claim 1". Multiple nucleic acids are referenced in claim 1, and it is not clear which one nucleic acid is being referred to in claim 22. In the absence of clarity, the metes and bounds of the claimed invention cannot be determined.

Drop

Claim 23 is further indefinite in its recitation of "The nucleic acid of Claim 1". Multiple nucleic acids are referenced in claim 1, and it is not clear which one nucleic acid is being referred to in claim 23. In the absence of clarity, the metes and bounds of the claimed invention cannot be determined. Claim 23 is further indefinite in its recitation of "the sequence that hybridized". Again, it is unclear if this refers to one of the many previously referenced sequences, or to a new, specific sequence. Furthermore, the use of "hybridized" in the past tense renders it unclear if only one sequence actually hybridized, and that is the sequence being claimed, or if multiple sequences

Drop

that hybridize with a sequence defined in (a) are possible. In the absence of guidance in the specification, the metes and bounds of the claimed invention cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(a) and 102(b) as being anticipated by Schulte et al. (1999), or Celniker et al. (1998), or Liao et al. (1998), or Vogel et al. (1998). Claim 1(a) reads on a nucleic acid which comprises a sequence selected from the sequences according to SEQUENCE ID NO: 1, SEQUENCE ID NO: 3, or SEQUENCE ID NO: 5. Schulte et al. disclose a sequence (Genbank Accession Number AF143846) identified as Helothis virescens putative nicotinic acetylcholine receptor alpha 7-2 subunit mRNA which has 97.8% identity and 100% best local similarity with SEQUENCE ID NO: 3 of the instant application over the entire length of the sequence, including between position 432 and position 1318. Schulte et al. also disclose a sequence (Genbank Accession Number AF143847) identified as Helothis virescens putative nicotinic acetylcholine receptor alpha 7-2 subunit mRNA, which has 97.4% identity and

100% best local similarity with SEQUENCE ID NO: 5 of the instant application over the entire length of the sequence, including between position 154 and position 1123.

Celniker et al. disclose a sequence (Genbank Accession Number AC004326) identified as Drosophila melanogaster DNA Sequence (Pi DS05899 (D22)), which has 100% best local similarity with the nucleotide sequence of SEQUENCE ID NO: 1 of the instant application, over a length of 210 bases, which is at least 14 bases in length.

Liao et al. disclose a sequence (Genbank Accession Number AF045432) identified as Danio rerio stem cell leukemia protein (tal-1) mRNA, which has 100% best local similarity with the nucleotide sequence of SEQUENCE ID NO: 3 of the instant application, over a length of 79 bases, which is at least 14 bases in length.

Vogel et al. disclose a sequence (Genbank Accession Number Z97178) identified as Beta vulgaris cDNA for elongation factor 2, which has 100% best local similarity with the nucleotide sequence of SEQUENCE ID NO: 5 of the instant application, over a length of 98 bases, which is at least 14 bases in length.

Therefore, the nucleotide sequences of Schulte et al., Celniker et al., Liao et al., and Vogel et al. meet the limitations of the claimed invention of claim 1 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-7, and 24-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schulte et al. or Celniker et al., or Liao et al, or Vogel et al., further in view of Ausubel et al.

The claims are drawn to vectors and host cells comprising the nucleic acids of the invention. Schulte et al., Celniker et al., Liao et al., and Vogel et al. anticipate the nucleic acid sequences of claim 1, upon which claims 2-7 and 24-31 depend. Claim 1(a) reads on a nucleic acid which comprises a sequence selected from the sequences according to SEQUENCE ID NO: 1, SEQUENCE ID NO: 3, or SEQUENCE ID NO: 5. Schulte et al. disclose a sequence (Genbank Accession Number AF143846) identified as Helothis virescens putative nicotinic acetylcholine receptor alpha 7-2 subunit mRNA which has 97.8% identity and 100% best local similarity with SEQUENCE ID NO: 3 of the instant application over the entire length of the sequence, including between position 432 and position 1318. Schulte et al. also disclose a sequence (Genbank Accession Number AF143847) identified as Helothis virescens putative nicotinic acetylcholine receptor alpha 7-2 subunit mRNA, which has 97.4% identity and 100% best local similarity with SEQUENCE ID NO: 5 of the instant application over the entire length of the sequence, including between position 154 and position 1123.

Celniker et al. disclose a sequence (Genbank Accession Number AC004326) identified as Drosophila melanogaster DNA Sequence (Pi DS05899 (D22)), which has 100% best local similarity with the nucleotide sequence of SEQUENCE ID NO: 1 of the instant application, over a length of 210 bases, which is at least 14 bases in length.

Liao et al. disclose a sequence (Genbank Accession Number AF045432) identified as Danio rerio stem cell leukemia protein (tal-1) mRNA, which has 100% best local similarity with the nucleotide sequence of SEQUENCE ID NO: 3 of the instant application, over a length of 79 bases, which is at least 14 bases in length.

Vogel et al. disclose a sequence (Genbank Accession Number Z97178) identified as Beta vulgaris cDNA for elongation factor 2, which has 100% best local similarity with the nucleotide sequence of SEQUENCE ID NO: 5 of the instant application, over a length of 98 bases, which is at least 14 bases in length. However, Schulte et al., Celniker et al., Liao et al., and Vogel et al. fail to specifically teach vectors and host cells comprising the various nucleic acids. However, at the time the claimed invention was made, Ausubel et al. taught the introduction of DNA into cells via vectors, thus anticipating vectors and host cells comprising nucleic acids. See chapter 9, especially page 9-1, 1st paragraph.

Extensive motivation to combine the references is taught by Ausubel et al., who teach many reasons to introduce a gene of interest into a cell. One motivating reason is that cell lines can be produced that over express the gene, allowing purification of the product for biochemical

characterization, or large-scale production of a product for pharmaceutical use. See page 9-1, first paragraph.

Therefore, it would have been *prima facie* obvious at the time the invention was made, for one of ordinary skill in the art to combine the above references and combine the nucleic acid sequences, as taught by Schulte et al., Celniker et al., Liao et al., or Vogel et al. with vectors and host cells comprising nucleic acids, as taught by Ausubel et al., to arrive at the vectors and host cells comprising the nucleic acids of the invention, of the claimed invention. Furthermore, one of ordinary skill in the art would have had a reasonable expectation of success, and introduced the nucleic acids of the instant invention into vector and host cells for the benefit of producing more of the nucleic acid of the instant invention, for example.

Conclusion

No claim is allowed, for the reasons outlined above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kris Pelham Mayo whose telephone number is (703) 306-5877. The examiner can normally be reached on Monday-Friday from 8:00 a.m. to 4:30 p.m. (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached at (703)308-0447. The FAX phone number for group 1600 is (703)308-4242.

An inquiry of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is (703)308-0196.

Kris Pelham Mayo, D.V.M.
Patent Examiner
Art Unit 1633
January 31, 2000

Karen M. Hauda
Karen M. Hauda
Patent Examiner